REMARKS

This Amendment is responsive to the Advisory Action dated March 6, 2002. At the outset, applicants note that the claims have been amended to reflect the elected invention, which was limited to the species of *in vivo* maintenance of stem cells with a further species election of providing a nucleic acid encoding Dpp to accomplish the claimed methods. Specifically, the Examiner requires that the preamble of claim 1 match the result of the recited steps in order to satisfy the requirements of 35 U.S.C. §112, second paragraph. Applicants have adopted the Examiner's suggestion by amending claim 1 as shown above. In addition, Applicants have changed "a population comprised of" to "a population comprising" to ensure that the "population" recited in the claims may be construed to encompass non-stem cells in view of the new dependent claims suggested above.

Furthermore, the Examiner finds claim 25 to be allegedly unclear as to whether the second host contains the necessary elements to affect the method of claim 1. In response, Applicants have amended claim 25 to clarify that transfer to a second host is for transplantation purposes as discussed on page 12, lines 8-9, and not for the purpose of increasing the abundance of stem cells in the second Drosophila as interpreted by the Examiner.

Moreover, applicants respectfully request rejoinder of claims 12, 13 and 17 with the elected invention. The Examiner explains in the second paragraph on page 2 of the Advisory Action that claims 12 and 13 were interpreted to encompass stimulating a pathway by the BMP receptor, which the Examiner regards as being part of group 4(c)(iv) while claim 17 was interpreted to encompass groups 4(e)(i) and (ii).

Applicants respectfully disagree with the Examiner's position because claims 12, 13 and 17 fall within the elected invention for the following reasons. Claim 12,

for instance, does not state that the pathway is stimulated "by" a BMP receptor but rather states that stimulation occurs "through" a BMP receptor. Stimulation through a BMP receptor occurs upon exposure to Dpp, which is expressed from a *dpp* nucleic acid. Thus, claim 12 defines a further portion of the BMP signaling pathway that is active upon expression of Dpp. Claim 13 is directed to the BMP receptor of claim 12 which may be selected from the group consisting of saxophone, Thick veins, and Punt as disclosed on page 3, lines 16-20.

Similarly, claim 17 is directed to a method according to claim 1 wherein BMP (Dpp) expression is increased by *hedgehog*- or *wingless*-activated transcription. Thus claim 17 recites one method of providing for expression of a nucleic acid encoding Dpp as discussed at the paragraph bridging pages 15 and 16 and as elected in the present application, and should therefore be included in the claims currently undergoing examination.

Thus, Dpp may be expressed in a variety of ways so as to increase the abundance of stem cells in Drosophila as illustrated in the new claims 44-50. Claim 44 is directed to the method of claim 1 and further defines the expression system used to provide Dpp as disclosed on page 12, lines 16-21.

New claims 45 and 46 are directed to claim 16 wherein said BMP signaling pathway is stimulated by increasing expression of Dpp in a stem cell or non-stem cell, respectively, of said population. Support for new claim 45 may be found on page 9, lines 24-25. Support for claim 46 may be found on page 11, lines 1-2, where the specification states that a BMP according to the invention is preferably secreted by non-stem cells and binds to receptors of stem cells to stimulate BMP signaling. New claim 50 is directed to new claim 46 and further specifies that the Dpp secreted by the

non-stem cell binds to a BMP receptor of a stem cell to stimulate the BMP signaling pathway as disclosed on page 11, lines 1-2.

Claim 47 is also dependent on new claim 46 and specifies that the non-stem cell is an ovarian somatic cell as discussed on page 18, lines 22-23. New claim 48 is dependent on new claim 47 and finds support in Example 7 in the paragraph bridging pages 23-24. New claim 49 defines the somatic follicle cell of new claim 48 as being an anterior somatic follicle cell as discussed on page 3, lines 12-14, where the specification indicates that Dpp is expressed in an anterior subset of follicle cells.

Finally, according to the last paragraph of the Advisory Action, bridging pages 2 and 3, the Examiner agrees that the expression of Dpp resulting in an increased number of stem cells in Drosophila was an unexpected observation that was not recognized in the prior art. However, the Examiner believes that the claims are still not drafted in a manner that distinguishes the claimed methods from those in the prior art. Specifically, the Examiner alleges that the specific type or amount of expression of Dpp that results in the unexpected outcome is not set forth in the claims.

Applicants respectfully disagree with the Examiner's position that the specific type or amount of expression of Dpp needs to be specified in the claims to distinguish over the prior art so long as the unexpected outcome of an increased abundance of stem cells is specified in the claims. The prior art references do not teach an increased abundance of stem cells either literally or inherently, as argued in the previous Amendment dated February 19, 2002 (see pages 12-21), so they do not anticipate or render obvious a method of increasing the abundance of stem cells in Drosophila notwithstanding the lack of specifically recited methodology.

Furthermore, the dependent claims recite a number of specific embodiments in which Dpp expression can be affected so as to accomplish the method recited in claim

1. For example, claims 16 and 17 specify that the method may be accomplished by increasing expression of endogenous Dpp, for instance by increasing expression of Dpp in a cell of the population recited in claim 1 (claim 16). Claim 8 specifies that Dpp expression may be increased by mutating a DPP gene to a gain-of-function phenotype thereby leading to greater signaling activity. And new claim 40 specifies that Dpp is ectopically expressed in the germarium of the host Drosophila using hsp70-GAL4 and UAS-*dpp*. Thus, Applicants respectfully argue that, with the knowledge of the present invention in hand, the skilled artisan may express Dpp in a variety of ways so as to increase the abundance of stem cells in Drosophila. Accordingly, Applicants respectfully request the withdrawal of the 35 U.S.C. §102 and 103 rejections.

CONCLUSION

Applicants respectfully submit that no new prohibited matter has been introduced by this Preliminary Amendment. This Reply is fully responsive to the Advisory Action dated March 6, 2002. Applicants respectfully request that the amended claims submitted herewith be entered along with the After Final amendments submitted in the previous Amendment dated February 19, 2002. The Examiner is urged to contact the undersigned regarding further issues or questions raised by this Reply, so that an allowance of the claimed subject matter may be expedited.

Except for issues payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to

Deposit Account 50-0310. This paragraph is intended to be a **constructive petition for extension of time** in accordance with 37 C.F.R. 1.136(a)(3).

Respectfully submitted
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APPENDIX

Amended claims showing changes made:

1. (Twice Amended) A method for [maintaining] increasing the abundance of germline stem cells of Drosophila *in vivo* comprising:

(a) providing a population [comprised of] comprising germline stem cells in a host Drosophila; and

(b) stimulating signal transduction of a bone morphogenetic protein (BMP) signaling pathway in at least one germline stem cell of said population by providing expression of a nucleic acid encoding Decapentaplegic (Dpp) protein;

wherein said stimulation increases the abundance of germline stem cells in said population as compared to a population in which signal transduction of said BMP signaling pathway has not been stimulated.

25. (Twice Amended) A method of autologous transplantation comprising transferring at least one germ line stem cell produced by the method according to Claim 1 [further comprising transferring at least one of said stimulated germ line stem cells] into a second host Drosophila.